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Abstract

²²⁵Ac complexes comprising a functionalized polyazamacrocyclic chelant compound of the formula I hereinbelow:

$$G \xrightarrow{Q} N \xrightarrow{T} Q$$
 $Q \xrightarrow{(I)} Q$

wherein:

T is

 \nearrow N

G is independently hydrogen or

$$L \xrightarrow{\begin{pmatrix} X \\ \downarrow \\ Y \end{pmatrix}_m} (CH_2)_n - C \xrightarrow{\downarrow} (CH_2)_r \xrightarrow{}$$

each Q is independently hydrogen, (CHR $^5)_{\,p} CO_2 R$ or (CHR $^5)_{\,p} PO_3 R^6 R^7$ or

$$L \xrightarrow{\begin{pmatrix} X \\ | \\ C \\ Y \end{pmatrix}_m} (CH_2)_n \xrightarrow{Q^1} (CH_2)_r \xrightarrow{\qquad}$$

 Q^1 is hydrogen, $(CHR^5)_wCO_2R$ or $(CHR^5)_wPO_3R^6R^7$; each R is independently hydrogen, benzyl or C_1-C_4 alkyl; R^6 and R^7 are independently H, C_1-C_6 alkyl or $(C_1-C_2$ alkyl) phenyl;

each R^5 is independently hydrogen; C_1-C_4 alkyl or $(C_1-C_2$ alkyl)phenyl;

with the proviso that at least two of the sum of Q and Q^1 must be other than hydrogen;

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A is CH, N, C-Br, C-Cl, C-SO₃H, C-OR⁸, C-OR⁹N⁺-R¹⁰X⁻, or

$$C-C\equiv C-\sqrt{}-R^{11}$$

Z and Z 1 independently are CH, N, C-SO_3H, N $^+-R^{10}X^-$, C-CH_2- OR^{8} or C-C(O)- R^{11} ;

 $\ensuremath{R^8}$ is H, $\ensuremath{C_{1}\text{--}C_{5}}$ alkyl, benzyl, or benzyl substituted with 5 at least one R12;

 R^9 is C_1 - C_{16} alkylamino;

 R^{10} is $C_1 - C_{16}$ alkyl, benzyl, or benzyl substituted with at least one R12;

 R^{11} is $-O-(C_1-C_3$ alkyl), OH or NHR¹³; R^{12} is H, NO_2 , NH_2 , isothiocyanato, semicarbazido, 10 thiosemicarbazido, maleimido, bromoacetamido or carboxyl;

 R^{13} is C_1-C_5 alkyl;

 ${\tt X}$ and ${\tt Y}$ are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-15 carbon bond;

n is 0 or 1;

m is an integer from 0 to 10 inclusive;

p is 1 or 2; 20 r is 0 or 1;

w is 0 or 1;

with the proviso that n is only 1 when X and/or Y form an additional carbon-carbon bond, and the sum of r and

w is 0 or 1; 25

L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being represented by the formula

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$$R^{1}$$
 $(Cyc)_{s}$ $(CH_{2})_{t}$

wherein:

s is an integer of 0 or 1; t is an integer of 0 to 20 inclusive; R¹ is H or an electrophilic or nucleophilic moiety which allows for covalent attachment to a biological carrier, or synthetic linker which can be attached to a biological carrier, or precursor thereof; and Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to a biological carrier; with the proviso that when R¹ is H, the linkage to the biological carrier is through one of Q or Q1; and with the proviso that when ${\ensuremath{R}}^1$ is other than H, at least one of Q and Q^1 must be $(CHR^5)_pPO_3R^6R^7$; and with further proviso that when Q is $(CHR^5)_pCO_2R$, Q^1 is $(CHR^5)_wCO_2R$, R is H, R^5 is H, and R^1 is H, then the sum of m, n, p, r,

or pharmaceutically acceptable salts thereof; complexed with $^{\rm 225}{\rm Ac}\,.$

s, t, and w is greater than 1;